### FIGURE 1

GCTCCCAGCCAAGAACCTCGGGGCCGCTGCGCGGTGGGGAGGAGTTCCCCGAAACCCGGCCG  $\tt CTAAGCGAGGCCTCCTCCCGCAGATCCGAACGGCCTGGGCGGGTCACCCCGGCTGGGA$ CAAGAAGCCGCCGCCTGCCTGCCCGGGCCCGGGGAGGGGGCTGGGGCCTGGGGCCGGAGGCGG TGTCTTGGGCACCTACCCGTGGGGCCCGTAAGGCGCTACTATATAAGGCTGCCGGCCCGGAG CCGCCGCGCCGTCAGAGCAGGAGCGCTGCGTCCAGGATCTAGGGCCACGACCATCCCAACCC GGCACTCACAGCCCCGCAGCGCATCCCGGTCGCCCCAGCCTCCCGCACCCCCATCGCCGG  ${\tt AGCTGCGCCGAGAGCCCCAGGGAGGTGCC} \underline{{\tt ATG}} {\tt CGGAGCGGGTGTGTGGTGCCACGTATGG}$ ATCCTGGCCGGCCTCTGGCTGGCCGTGGCCGGCCCCCTCGCCTTCTCGGACGCGGGCC CCACGTGCACTACGGCTGGGGCGACCCCATCCGCCTGCGGCACCTGTACACCTCCGGCCCCC ACGGGCTCTCCAGCTGCTTCCTGCGCATCCGTGCCGACGGCGTCGTGGACTGCGCGCGGGGC CAGAGCGCGCACAGTTTGCTGGAGATCAAGGCAGTCGCTCTGCGGACCGTGGCCATCAAGGG  ${\tt CGTGCACAGCGTGCGTACCTCTGCATGGGCGCCGACGGCAAGATGCAGGGGCTGCTTCAGT}$ ACTCGGAGGAAGACTGTGCTTTCGAGGAGGAGATCCGCCCAGATGGCTACAATGTGTACCGA TCCGAGAAGCACCGCCTCCCGGTCTCCCTGAGCAGTGCCAAACAGCGGCAGCTGTACAAGAA CAGAGGCTTTCTTCCACTCTCATTTCCTGCCCATGCTGCCCATGGTCCCAGAGGAGCCTG AGGACCTCAGGGGCCACTTGGAATCTGACATGTTCTCTTCGCCCCTGGAGACCGACAGCATG  ${\tt GACCCATTTGGGCTTGTCACCGGACTGGAGGCCGTGAGGAGTCCCAGCTTTGAGAAG} {\color{red}{\bf TAA}CT} {\color{blue}{\bf CT}} {\color{blue}{\bf C$ TGCTTCTACAAGAACAGTCCTGAGTCCACGTTCTGTTTAGCTTTAGGAAGAAACATCTAGAA GTTGTACATATTCAGAGTTTTCCATTGGCAGTGCCAGTTTCTAGCCAATAGACTTGTCTGAT CATAACATTGTAAGCCTGTAGCTTGCCCAGCTGCTGCCTGGGCCCCCATTCTGCTCCCTCGA GGTTGCTGGACAAGCTGCTGCACTGTCTCAGTTCTGCTTGAATACCTCCATCGATGGGGAAC TCACTTCCTTTGGAAAAATTCTTATGTCAAGCTGAAATTCTCTAATTTTTTCTCATCACTTC CCCAGGAGCAGCCAGAAGACAGGCAGTAGTTTTAATTTCAGGAACAGGTGATCCACTCTGTA AAACAGCAGGTAAATTTCACTCAACCCCATGTGGGAATTGATCTATATCTCTACTTCCAGGG GCTTCAGGAGTAGGGGAAGCCTGGAGCCCCACTCCAGCCCTGGGACAACTTGAGAATTCCCC  $\tt CTGAGGCCAGTTCTGTCATGGATGCTGTCCTGAGAATAACTTGCTGTCCCGGTGTCACCTGC$ TTCCATCTCCCAGCCCACCAGCCCTCTGCCCACCTCACATGCCTCCCCATGGATTGGGGCCT CCCAGGCCCCCACCTTATGTCAACCTGCACTTCTTGTTCAAAAATCAGGAAAAGAAAAGAT TTGAAGACCCCAAGTCTTGTCAATAACTTGCTGTGTGGAAGCAGCGGGGGAAGACCTAGAAC TTTTGTATATTAAAATGGAGTTTGTTTGT

### · FIGURE 2

MRSGCVVVHVWILAGLWLAVAGRPLAFSDAGPHVHYGWGDPIRLRHLYTSGPHGLSSCFLRI RADGVVDCARGQSAHSLLEIKAVALRTVAIKGVHSVRYLCMGADGKMQGLLQYSEEDCAFEE EIRPDGYNVYRSEKHRLPVSLSSAKQRQLYKNRGFLPLSHFLPMLPMVPEEPEDLRGHLESD MFSSPLETDSMDPFGLVTGLEAVRSPSFEK

signal peptide:

amino acids 1-22

N-myristoylation sites:

amino acids 15-21, 54-60, 66-72, 201-207

Prokaryotic membrane lipoprotein lipid attachment site:

amino acids 48-59

HBGF/FGF domain:

amino acids 80-131

FIGURE 3A

FIGURE 3B

Leptin (mg/ml)

1-7

1-7

RGF19 wild type

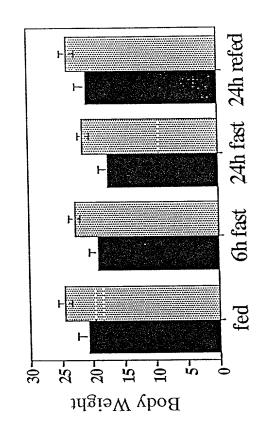
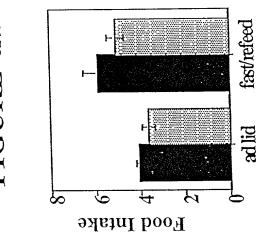


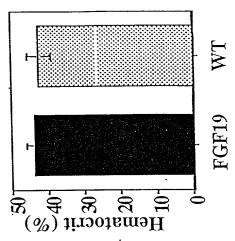
FIGURE 4B

FIGURE 4A



Water Intake ml/day

WT FGF19



1.5-

0.5

Urine output (ml/day)

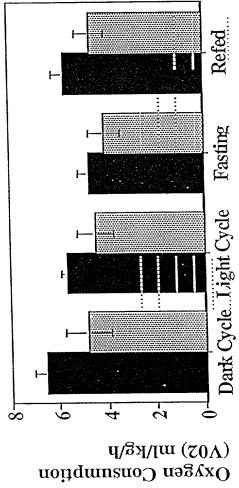
FIGURE 4D

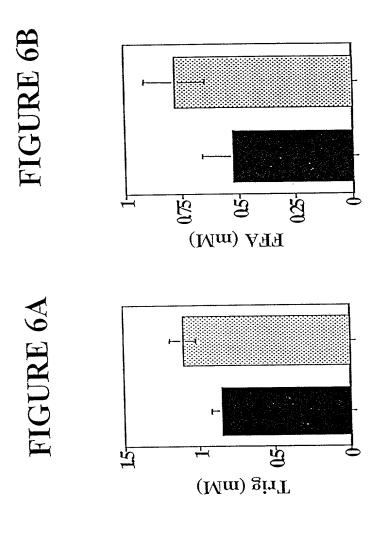


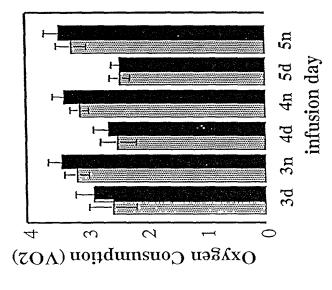
WT

FGF19

FIGURE 5







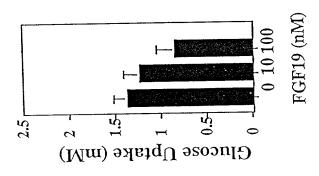
3-

food intake (g/d)

7

infusion day





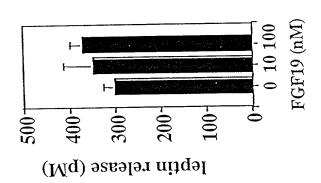
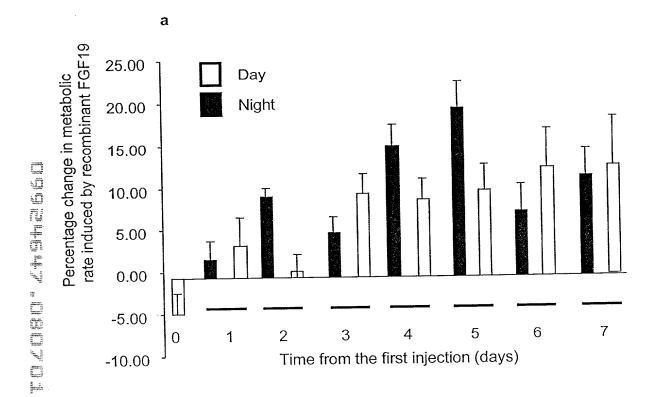
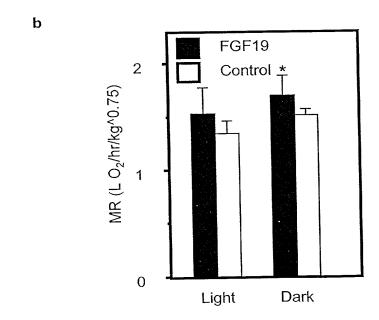


FIGURE 9

FIGURE 10

Fig. 11





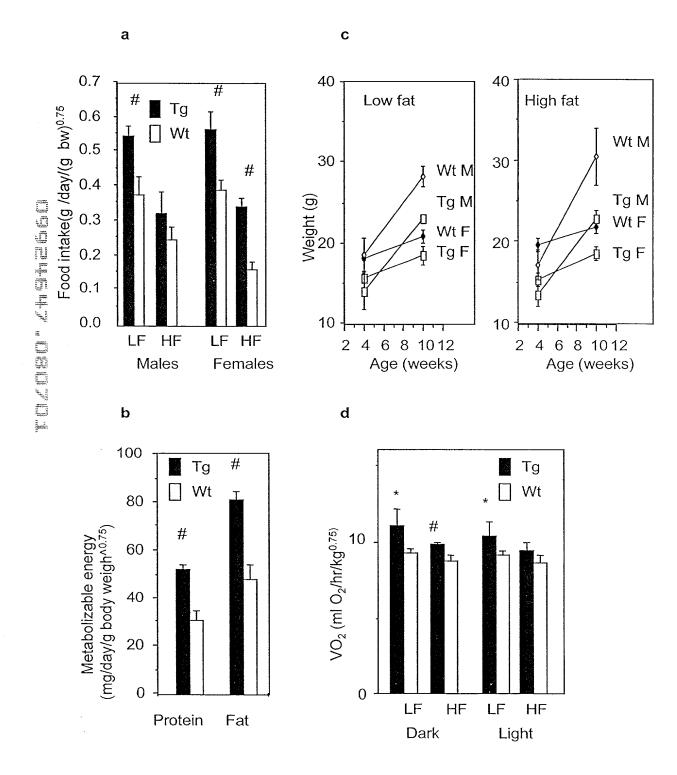
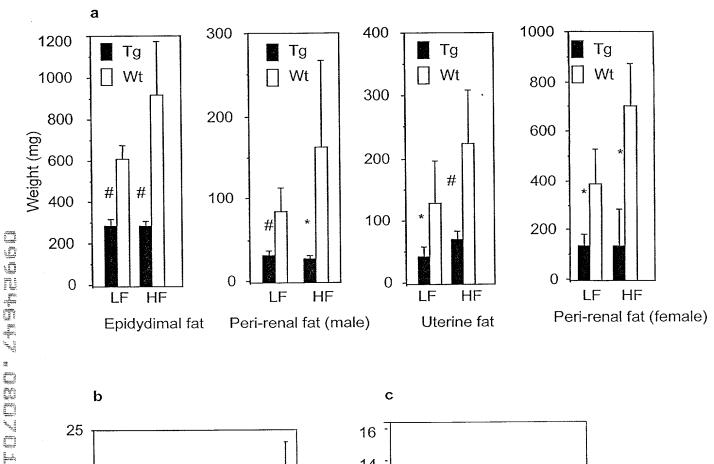
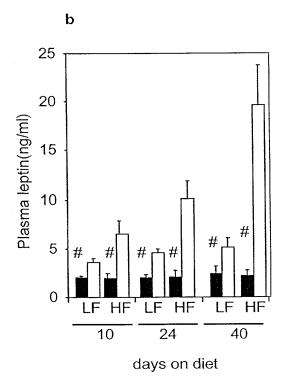


Fig. 13





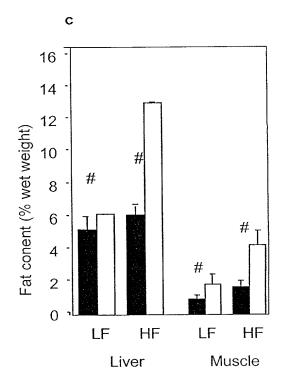
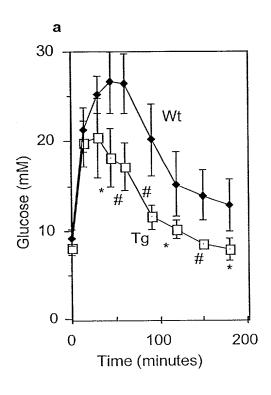
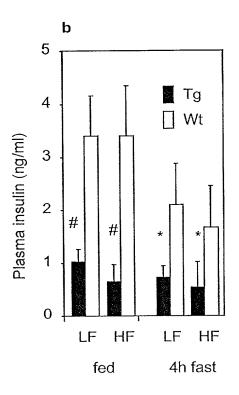
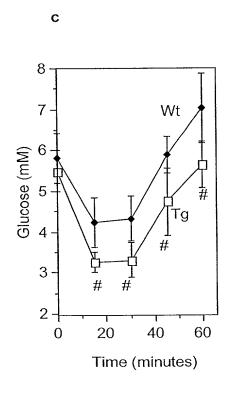
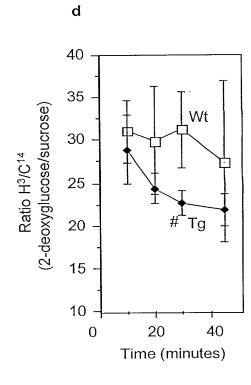


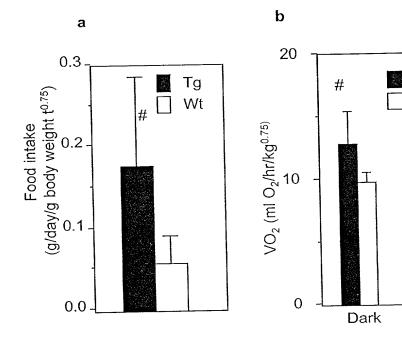
Fig. 14.









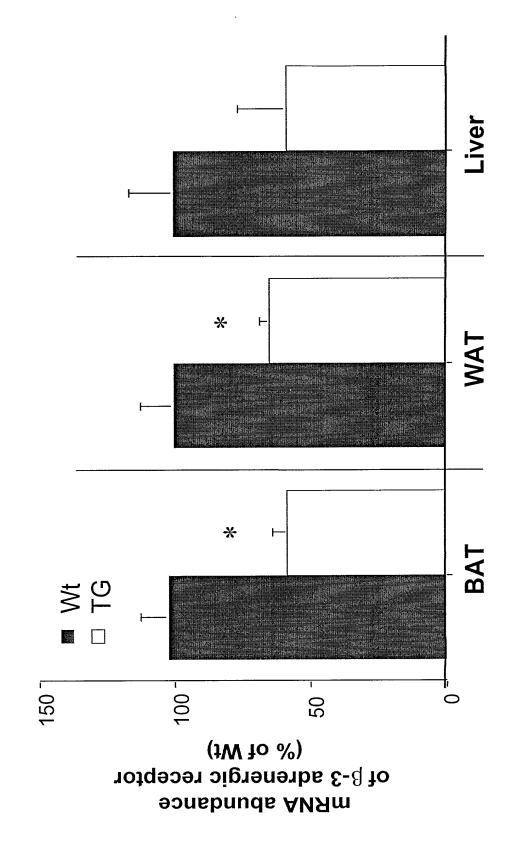


Tg Wt

Light

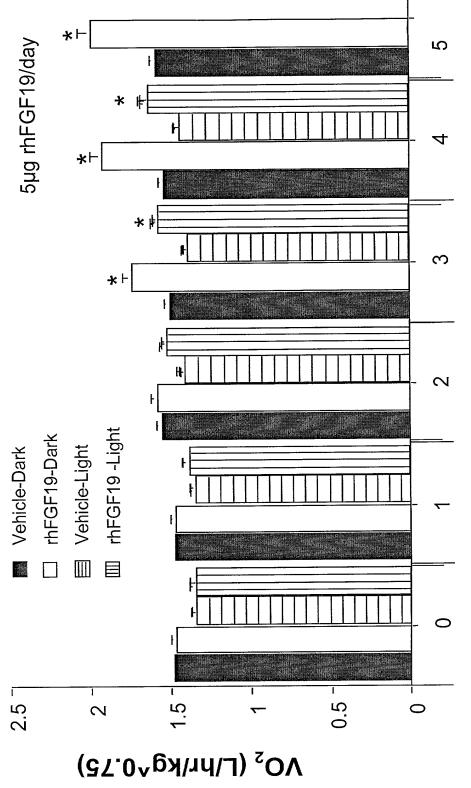
#

Figure 16



\*P < 0.05 vs Wt controls

## Figure 17



# Time from the first injection (days)

\*P < 0.05 vs Vehicle controls with the same cycle on the same day

Figure 18

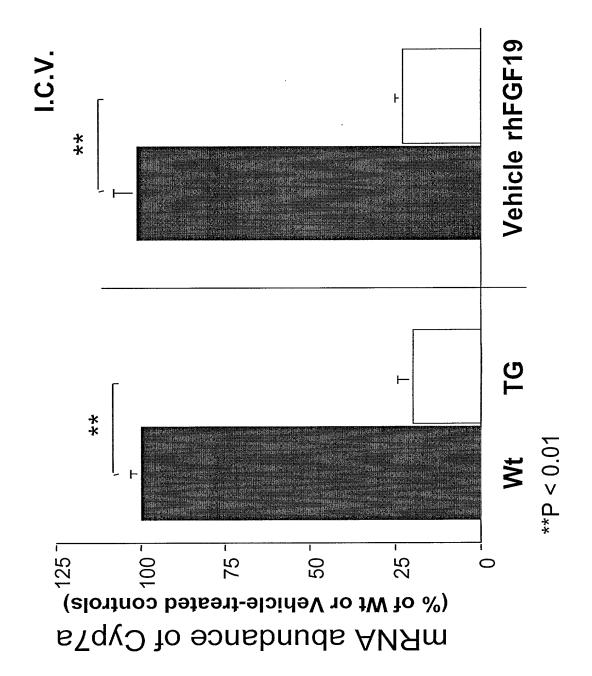
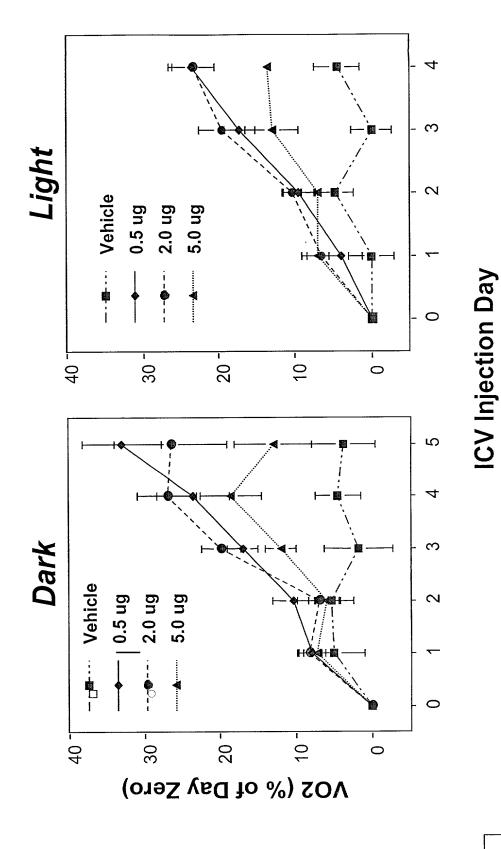


Figure 19



### Figure 20

		<b>S</b>	rhFGF19	
	Vehicle	5.0 µg	2.0 µg	0.5 µg
NPY	1.0 +/- 0.08	0.81 +/- 0.23	0.63 +/-0.20	0.40 +/- 0.08
AgRP	1.0 +/- 0.33	0.26 +/- 0.10	0.57 +/- 0.26	0.29 +/- 0.16
POMC	1.0 +/- 0.27	1.49 +/- 0.42	3.48 +/- 1.5	38.77 +/- 3.32
MC4-R	1.0 +/- 0.16	0.47 +/- 0.09	0.70 +/- 0.10	0.48 +/- 0.08